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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/920,137	08/01/2001	George Heavner	CEN0250	5801

27777 7590 01/05/2004

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EXAMINER
SEHARASEYON, JEGATHEESAN

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 01/05/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/920,137	HEAVNER ET AL.	
	Examiner	Art Unit	
	Jegatheesan Seharaseyon	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 October 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,9 and 16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,9 and 16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a)☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6/17& 8/26* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. This Office Action is response to Applicant's election of Group I, claims 1-3, 9-11, 16, 21-23, 29-31, 36, 41-43, 49-51, 56, 61-63, 69-71, 76, 81-83, 91 and 96 drawn to protein and compositions. Election was made without traverse in the response filed on 10/14/03. Applicant has further elected to cancel claims 4-8, 10-15 and 17-101.

However, Applicant has traversed the requirement for sequence election on the basis that all of these sequences (SEQ ID NO: 1-8) relate to the variable regions or the CDRs of a single antibody fragment comprising the heavy and light chain variable regions or CDR regions. This is not found to be persuasive because regardless of the nature of the TNF antibody generated, sequences SEQ ID NO: 7 (depicts MIP-1b) and SEQ ID NO: 8 (depicts RANTES) are for chemokines, thus TNF antibodies containing these sequences are structurally and functionally different. Contrary to Applicants assertion, SEQ ID NO: 7 and 8 are not drawn to the heavy and light variable regions. Therefore, the searches for each of the different antibodies are not coextensive and would be a burden on the office to search all of the different sequences. Thus, a TNF antibody comprising SEQ ID NO: 7 will be searched. Therefore, the restriction requirement is deemed proper and made FINAL.

Specification

2. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

3.The disclosure is objected to because of the following informalities: The blanks present throughout the specification. It is also not clear what is referred by the symbol TNF∀ throughout the specification. Appropriate correction is required.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-3, 9 and 16 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

4a. Claims 1-3, 9 and 16 are rejected as vague and indefinite because Applicant is indicating that SEQ ID NO: 7 and 8 are drawn to variable regions. However, the sequences provided are for MIP-1b and RANTES chemokines. Claims 2 and 3 are rejected insofar as they depend on claim 1. For the purpose of examination it is assumed that the claims are directed anti-TNF antibodies.

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5a. Claims 1, 9 and 16 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for TNF antibody comprising a heavy or light variable region, does not reasonably provide enablement for comprising at least SEQ ID NO: 7 (MIP-1b) and SEQ ID NO: 8 (RANTES) as a variable region. The specification does not

enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. See *In re Wands,* 858 F.2d at 737, 8 USPQ2d at 1404. The factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: (1) the breadth of the claims; (2) the nature of the invention; (3) the state of the prior art; (4) the level of one of ordinary skill; (5) the level of predictability in the art; (6) the amount of direction provided by the inventor; (7) the existence of working examples; and (8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

Claims 1, 9 and 16 are drawn to an anti-TNF antibody having at least one variable region comprising SEQ ID Nos: 7 and 8. The specification defines SEQ ID Nos: 7 and 8 as variable regions (see paragraph 72, line 23). The specification also states that the anti-TNF antibody comprises at least of heavy chain variable region, optionally having the amino acid sequence of SEQ ID NO: 7 and/or at least one light chain variable region, optionally having the amino acid sequence of SEQ ID NO: 8 (see paragraph 105, lines 16-20). However, the sequence listing provides the SEQ ID NO: 7 (MIP-1b) and SEQ ID NO: 8 (RANTES) polypeptide sequences. Virtually all polypeptides are immunogenic when exposed to various organisms' immune systems;

the specification does not provide meaningful structural or functional limitations for "an anti-TNF antibody with MIP-1b or RANTES as a variable region."

Table 1 discloses several antibodies with variable regions. The specification suggests making antibodies that specifically bind TNF polypeptides, useful in treatment and diagnosis. Although no antibodies comprising anti-TNF antibody with MIP-1b or RANTES as a variable region are presented as working examples, such can be made routinely in the art. However, the specification does not teach how to use these TNF antibodies comprising the chemokines as variable regions. The usefulness of the antibody or binding compound is tied to the usefulness of the polypeptide it specifically binds. In the instant application, there is insufficient guidance regarding how to making anti-TNF antibodies with MIP-1b or RANTES as variable regions. The problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. Applicant has provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to generate the antibodies. Although the specification outlines art-recognized procedures for producing chimeric antibodies, this is not adequate guidance as to the nature of active derivatives that may be constructed, but is merely an invitation to the artisan to use the current invention as a starting point for further experimentation.

A large quantity of experimentation would have been necessary for the skilled artisan to generate the anti-TNF antibodies with MIP-1b or RANTES as variable regions recited in the claims and possibly screen the same for a useful activity, and then

generate specific binding compounds to same. The specification fails to provide sufficient direction/guidance regarding which structural features are required in order to provide anti-TNF antibodies with MIP-1b or RANTES as variable regions for activity. There are no working examples directed anti-TNF antibodies with MIP-1b or RANTES as variable regions. The nature of the invention is complex, involving the generation of l anti-TNF antibodies with MIP-1b or RANTES as variable regions and screening them for a useful activity. The state of the prior art establishes the unpredictability of the effects of chimeric antibodies. Finally, the breadth of the claims is large, failing to recite any structural or functional limitations. For all of these reasons, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6a. Claims 1-3, 9 and 16 are rejected under 35 U.S.C. 102(b) as being anticipated by Le et al. (U.S. Patent NO: 5, 656, 272).

The instant invention is directed to anti-TNF antibody comprising variable regions.

Le et al. describe anti-TNF antibody comprising a variable region (column 28-30). The affinity of TNF antibody is at least 10^{-9} M (column 36, lines 1-5). Le et al. also teach

that the antibody is capable of blocking TNF-induced IL-6 secretion (column 36, lines 5-15), thus meeting the limitation of instant claim 3. In addition it also teaches the compositions with pharmaceutically acceptable carriers (column 36, lines 23-40). In addition, it also teaches various methods of administration of the TNF antibody including parenteral, oral, intravenous and intramuscular (column 35, lines 10-24). It further describes a device to infuse the chimeric antibody into a patient (column 58, lines 44-53). Therefore, claims 1-3, 9 and 16 are rejected under 35 U.S.C. 102(b) as being anticipated by Le et al. (U.S. Patent NO: 5, 656, 272).

7. No claims are allowable over prior art.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jegatheesan Seharaseyon whose telephone number is 703-305-1112. The examiner can normally be reached on M-F: 8:30-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on 703-308-4623. The fax phone number for the organization where this application or proceeding is assigned is 703-308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

LORRAINE SPECTOR
PRIMARY EXAMINER

JS